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EDITORIAL COMMENTARY

Advancements in the mind-machine interface: towards re-establishment of direct cortical control of limb movement in spinal cord injury

Spinal cord injury (SCI) resulting in loss of motor function can be caused by a variety of conditions, ranging from traumatic to neoplastic to infectious. It is estimated that nearly 300,000 individuals live with the effects of SCI in the United States alone (National Spinal Cord Injury Statistical Center, 2016). Current treatment modalities for patients suffering from SCI are primarily supportive, with no therapeutic options for restoration of significant function (Thuret et al., 2006). In addition to the devastating effects on individual patients, the persistence of SCI-related deficits also leads to a significant economic impact. The most recent estimate of lifetime SCI-related costs for an American Spinal Injury Association Impairment Scale A patient with high tetraplegia is well over $4.5 million dollars (National Spinal Cord Injury Statistical Center, 2016).

Because of the high individual and societal burden of SCI, it is unsurprising that various therapeutic pathways have been pursued to ameliorate its effects. Broadly speaking, these approaches fall into one of three paradigms, which are all areas of intensive research. Neuroprotective approaches aim to preserve neural pathways. Other approaches aim to stimulate repair and regeneration of the injured spinal cord, thereby re-establishing the connection or providing a connection alternate to the one severed by the injury (Sahni and Kessler, 2010). Pursuit of this goal in recent years has primarily focused on promising small molecules as well as cellular transplantation approaches. Although some agents have shown great promise, we await phase III human studies. The third tactic is to use engineering approaches to bypass the injured spinal cord entirely, allowing for the resumption of motor function in spite of the SCI. This paradigm has seen the greatest advancement over the past decade as a result of innovations in engineering, material sciences, and mind–machine interface technologies.

In their recently published investigation, Bouton et al. (2016) chose the third approach, and their article describes pioneering work in utilizing an intracortical microelectrode array to drive—in real time—a previously paralyzed human arm through a neuromuscular electrical stimulation system. The patient, a 24-year-old man whose C_5 quadriplegia occurred after a diving accident 4 years earlier, was implanted with a microelectrode array over his motor cortex hand region, identified preoperatively with functional magnetic resonance imaging. Cortical electrical activity was converted into motor signals by using machine-learning algorithms, and this information was relayed to a high-resolution neuromuscular electrical stimulator. This stimulator, in the form of a wearable arm sleeve equipped with 130 electrodes, stimulated the patient's paralyzed limb and produced controlled movement in response to cortical signals. After over a year of regular training with the system, the subject was able to demonstrate reasonably accurate fine-motor movements of the digits and wrist, with an overall accuracy of 70.4%. More importantly, the patient was also able to utilize the system to perform a basic act of daily living—grabbing a bottle, pouring the contents into another container, and then stirring the contents with a stick. The authors concluded that, with the system in place, the patient's functional status improved from a C_5 injury to that of a T_1 injury, reflecting a substantial improvement in terms of the ability to function independently and to perform acts of daily living.

This work builds on several decades of investigation into mind–machine interfaces. One of the foundations of these investigations is the early work of Georgopoulos et al. (1986) that elucidated the directionality of neuronal groups within the motor cortex. By leveraging the information coded by these neurons, the intention to move may be translated and interpreted. While Bouton et al. (2016) utilized these data to drive electrical stimulation of the patient's native paralyzed limb, other groups have focused on using the mind–machine interface to drive a prosthetic limb; for example, Collinger et al. (2013) reported highly accurate real-time control by a tetraplegic patient of a bioprosthetic arm with 7 degrees of freedom through recordings obtained *via* an intracortical implant.

An additional bioengineering approach is also demonstrating great promise. This approach removes the dependence on cortical input altogether by employing the ability of the distal uninjured spinal cord to produce motor signals. The discovery of these "central pattern generators" (Grillner, 1985) formed the basis for investigations into the utility of epidural spinal cord stimulation to restore lower limb function. This research culminated in the work of Harkema et al. (2011), with the restoration of weight-bearing upright posture in a paraplegic subject by using epidural stimulation of the lumbosacral spine.

A further extension of bioengineering approaches even less dependent on the central nervous system is so-called "exoskeleton" technology. Effective exoskeletons are currently available for use by rehabilitation programs as a way to provide support during strenuous physical therapy activities and to minimize falls. Next-generation exoskeletons in development will utilize mind–machine interfaces to coordinate and guide movements of patients with SCI (To et al., 2014).

Despite these dramatic advances within the past decade, significant challenges remain before the overarching goal of restoring functional independence to SCI patients can be achieved. Possibly the most fundamental obstacle is the current need to obtain intracortical recordings to control these mind–machine interfaces. Surface electroencephalography is desirable so as to avoid a craniotomy with intracerebral implantation of electrodes; however, the increased artifact generated by the skull and lower resolution of the resulting signal presents significant challenges in accurate translation of the cortical signal.

The issue of signal degradation caused by induced gliosis around the cortical electrodes represents another major engineering hurdle. In their study, Bouton et al. noted a loss of 17 of 50 neural units in their recordings over the course of the study—over a third in total. Such signal loss can compromise the ability to record accurate signals and requires regular recalibration and adjustment of the decoding algorithm. Overcoming this obstacle will likely require advancements in both materials design and electrode machining.

Apart from the risks related to craniotomy for electrode implantation such as infection and cortical vessel injury, the transcutaneous nature of the interface connection in current systems makes the implant susceptible to complications such as skin breakdown and tissue overgrowth. Future systems will likely need to implement wireless solutions such as telemetry, both for longevity and to make day-to-day use feasible (Collinger et al., 2013). Finally, the technical expertise needed to implant these systems is nontrivial, requiring precise placement over the appropriate region of the motor strip (Bouton et al., 2016) and manipulation of delicate materials.

Another major limitation of current mind–machine interface technology is the lack of sensory feedback. From a mechanistic perspective, tactile and proprioceptive information plays a vital role in the control and regulation of motor movements. Current systems rely heavily on direct visualization for modulation of motor activities (Collinger et al., 2013; Bouton et al., 2016), but such control is both limited and impractical if the end goal is functional independence. Restoration of motor function without sensation will likely also present a safety barrier for adoption of such technology. One can imagine the issues that could arise, for example, if the grab–pour–stir experiment used in the Bouton study were re-enacted in the uncontrolled setting of a kitchen. These issues are, of course, all secondary to the desire of patients with SCI to not only mechanically manipulate their surroundings, but to truly interact with their environment as they did prior to their injury—something that is not possible without restoration of sensory as well as motor function. Research into restoration of afferent sensory feedback through bioprostheses is ongoing (Raspopovic et al., 2014), and it is likely that the next major paradigm shift in mind–machine interface technologies for SCI will involve the implementation of these technologies.

The totality of current research into mind–machine interface technologies in human subjects has been performed in a controlled, laboratory setting. The need for frequent recalibration of these systems, not to mention the unwieldy nature of the technologies driving the decoding and translation of cortical signals into movement, makes testing of these devices impractical in a more natural environment. Improved miniaturization is important, therefore, not only for the cortical implants themselves, but for the computing and control systems as well. A corollary of this is the extreme expense of these initial technologies. Although the high costs are unsurprising given the cutting-edge nature of the bioprostheses and implants being developed, any widespread benefit for the SCI community will be heavily dependent on whether such devices can be made available at a price point that healthcare payors can bear.

As such systems edge ever closer to more widespread use, the healthcare, rehabilitation, and psychosocial support system for SCI patients must be prepared to deal with the challenges that will inevitably result. Physicians who treat SCI patients must familiarize themselves with these technologies and be knowledgeable enough to recognize those who will benefit from their use. The healthcare system must also be prepared to manage the complications that will invariably arise as a result of mind-machine interface–related implants, such as infected hardware, software malfunctions, and other long-term complications about which, at present, we can only speculate. The intense training that these early patients need to utilize their prosthetics suggests that successful use of these systems in the future will be heavily reliant on a well-organized rehabilitation program. It will be imperative, therefore, that such programs evolve with bioprosthetic technologies so that patients can reap the maximum possible benefit from such devices. Lastly, appropriate psychosocial support for these patients will be crucial to help them navigate a return to greater independence, and, hopefully, to activities such as school and work.

The work by Bouton et al. (2016) represents a major step forward in the restoration of function for individuals with SCI. Although significant challenges remain before such technologies can be widely adopted, the rapid progress over the past decade inspires hope that, in the near future, we will not be forced to simply manage the complications resulting from SCI, but will be able to offer a return to independence for these patients.

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Jian Guan, Gregory W.J. Hawryluk*

Department of Neurosurgery, Clinical Neurosciences Center, University of Utah, Salt Lake City, UT, USA

***Correspondence to:** *Gregory W.J. Hawryluk, M.D., Ph.D., neuropub@hsc.utah.edu.*
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